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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,425	03/03/2006	Michel P Rathbone	BEP 3020	8737

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ALEXANDRIA, VA 22314

EXAMINER
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DUTT, ADITI

ART UNIT	PAPER NUMBER
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1649

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/24/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/531,425	RATHBONE ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Aditi Dutt	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 22 February 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) 4,5,8,9,13,14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 6-7,10-12, 15-16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-16 are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 April 2005 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some    \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>8/2/05</u> . | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

### *Status of Application, Amendments and/or Claims*

1. The amendment of 3 March 2006 in the claims has been entered in full.  
Claims 1-16 are amended.

### *Election/Restrictions*

2. Applicant's election of multiple sclerosis as the species of neurodegenerative disease, readable on claims 1-3, 6, 7, 10-12, and 15-16, in the reply filed on 22 February 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
3. Claims 4, 5, 8, 9, 13 and 14, are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 22 February 2007.
4. Claims 1-3, 6, 7, 10-12, and 15-16, are under consideration in the instant application.

***Oath/Declaration***

5. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. It was not executed in accordance with either 37 CFR 1.66 or 1.68. There is no date entered next to the signature of one of the inventors. Appropriate correction is required.

***Drawings***

6. The instant drawings do not comply with 37 C.F.R. § 1.84(U)(1), which states that partial views of a drawing which are intended to form one complete view, whether contained on one or several sheets, must be identified by the same number followed by a capital letter. Figure 3a of the instant application, for example, are presented on two separate panels. The two panels of drawings, which are labeled "Figure 3a" in the instant specification should be renumbered as "Figures 3A and 3B". Likewise, the two panels of Figure 3b should be renumbered as "Figure 3C and 3D", and Figure 3c should be "Figure 3E and 3F". Additionally, Figures 4a and 4b are each represented by 3 separate panels. The 3 panels of drawings for figures 4a and 4b should be relabeled as "Figure 4A, 4B and 4C" and "Figure 4D, 4E and 4F" respectively. Applicant is reminded that once the drawings are changed to meet the separate numbering requirement of

37 C.F.R. § 1.84(U)(1), Applicant is required to file an amendment to change the Brief Description of the Drawings and the rest of the specification accordingly.

### ***Specification***

7. The disclosure is objected to because of the following informalities:

#### **Arrangement of the Specification**

The specification is not arranged in the format specified in MPEP. Following guidelines should be followed:

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

- (a) TITLE OF THE INVENTION.
- (b) CROSS-REFERENCE TO RELATED APPLICATIONS.
- (c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
- (d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
- (e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
- (f) BACKGROUND OF THE INVENTION.
  - (1) Field of the Invention.
  - (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
- (g) BRIEF SUMMARY OF THE INVENTION.
- (h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
- (i) DETAILED DESCRIPTION OF THE INVENTION.

Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-3, 6-7, 10-12, 15-16, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
10. Claims 1 and 10 are rejected as being indefinite because it is not clear where and how the enteric glial cell will be administered. It is not clear if there is a step missing. For example, will it be administered to a subject, or to a culture medium, to a cell, or a tissue etc.?
11. Claims 2-3, 6-7, 11-12 and 15-16, are also rejected under 35 U.S.C. 112, second paragraph, as they depend from claims 1 and 10 for this limitation.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**Lack of Enablement**

12. Claims 6-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one

skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

13. The specification does not reasonably provide enablement for treating an individual having a neurodegenerative disease, such as multiple sclerosis, by administration of human enteric glial cells, and promoting functional regeneration of injured nerve fibres in the nervous system. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

14. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, include the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed. The instant disclosure fails to meet the enablement requirement for the following reasons:

15. The claims are drawn to a method of promoting functional regeneration of injured nerve fibres in the nervous system, thereby treating any neurodegenerative disease, such as multiple sclerosis, by administering an effective amount of an enteric glial cell.

16. The specification of the instant application teaches that the Type II enteric glial cells, derived from the enteric nervous system of the small intestine, have long processes, higher concentration of the glial fibrillary acidic protein (GFAP),

and properties similar to the central nervous system (CNS) astroglia (page 5, para 0027; page 9, para 0046). The specification demonstrates that the enteric glial cells transplanted into the spinal cord of animals, results in the migration and induction of the blood brain barrier formation after 2-3 months (pages 8-9, para 0041 (iii), (iv), Example 1; figures 3a, 3b, 4a, 4b). The specification also demonstrates the functional regeneration and connection of the cut nerve fibres following a spinal cord injury, by increased recovery of the cutaneous trunci muscle reflex, a behavioral test (figure 6). However, the specification does not disclose any methods or working examples for treating any neurodegenerative disease, for example multiple sclerosis (MS), by administering enteric glial cells. Undue experimentation would be required by one skilled in the art, to treat patients with all possible neurodegenerative disorders, by administering enteric glial cells.

17. Relevant literature of the art teaches that the enteric nervous system is the largest part of the peripheral nervous system (PNS), having a neuronal concentration similar to the spinal cord, but structurally and functionally more comparable to the CNS (Cabarrocas et al. *Glia* 41: 81-93, 2003; page 81, para 1; Gershon and Rothman, *Glia* 4: 195-204, 1991; page 196, column 1, para 2). The art also teaches that the transplantation of enteric glia to the injured spinal cord, can be useful for regenerating spinal afferents (Jaeger, *J Neur Transpl Plasticity* 5: 223-232, 1995; page 223, column 2, para 1). The art further teaches that MS is a complex neurological disease, characterized by the loss of CNS myelin



caused by an immune attack on the myelin sheaths and the myelin producing oligodendrocytes, resulting in multifocal demyelination (plaques) and inflammation, scattered throughout the white matter of the CNS (Tepavcevic and Blakemore, Phil Trans R Soc B 360: 1775-1795, 2005; page 1775, column 1, para 1; Stangel, Expert Opin Invest Drug 13: 331-347, 2004; page 331).

However, relevant prior and post art literature do not teach treating any neurodegenerative disorder, like multiple sclerosis, by administering enteric glial cells. Undue experimentation would also be required of one skilled in the art to treat all possible neurodegenerative diseases (claim 6) using this method.

18. The art further teaches that cell transplantation/administration, for the treatment of several neurodegenerative diseases such as Alzheimer's disease or epilepsy is difficult as these involve many types of neurons and neurotransmitters (Lindvall, Cell Transplantation, 4: 393-400, 1995). The art also teaches that the CNS myelination is more complicated than the peripheral nervous system myelination, and although studies on the remyelination of the CNS using the experimental autoimmune encephalomyelitis mouse model are conducted, a transition from animals to human patients is encountered with problems because of the lack of efficacy and unforeseen complications observed in complex immune-mediated diseases caused by an autoimmune attack against CNS components such as myelin, proteins and lipids (Fontoura et al. Int Rev Immunol 24: 415-446, 2005, abstract). Furthermore, significant differences are observed between the human CNS glia and rodent cells, whereby the data from the rodent

cell types cannot be directly extrapolated to the human cells, because of variations in cell phenotypes (Halfpenny et al. *Lancet Neurol* 1: 31-40, 2002; page 33, column 1, para 3; page 34). Finally the art summarizes the reasons for failures of clinical trials for the treatment of MS, employing administration of cells for inducing CNS remyelination, stating that the time and site of administration (i.e. the stage of the demyelination), limited migration of the cells, irreversible molecular changes in demyelinated axons, a progression of the astrocytic scar preventing further remyelination, and the difficulty to prevent axonal loss, are important factors that need experimentation for successful treatment of MS (Stangel, *J Neurol Neurosurg Psychiat* 72: 1-4, 2002; page 3, column 3, para 1; Halfpenny et al. page 32, column 1, para 5; column 2, para 1). Lastly, it is well known in the art that many neurodegenerative diseases are proven to be recalcitrant to treatment such as Alzheimer's Disease (Halliday et al *Clin Exp Pharmacol Physiol* 27: 1-8, 2000), Parkinson's Disease (Steece-Collier et al., *PNAS USA* 99(22): 13972-13974, 2002), Down's Syndrome (Appendix A), and Huntington's Disease (Feigin et al., *Curr Opin Neurol* 15: 483-489, 2002). As the molecular processes of pathogenesis of the various neurodegenerative diseases including multiple sclerosis are yet to be fully uncovered, the success of treatment would be unpredictable, thus the invention would entail undue experimentation by a skilled artisan. Therefore, one skilled in the art would not be able to predict from the instant specification that all possible neurodegenerative

diseases would be treated by administration of enteric glial cells. Undue experimentation would be required to determine such.

19. Due to the large quantity of experimentation necessary to treat any neurodegenerative disease by administering enteric glial cells; the lack of direction/guidance presented in the specification regarding the same; the absence of working examples directed to same; the complex nature of the invention; the state of the prior and post art which has yet to determine remyelination and repair of MS lesions and, the unpredictability of treatment of neurodegenerative diseases; undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

#### Scope of Enablement

20. Claims 10-12, 15-16, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inducing the formation of a blood brain barrier in the nervous system by the administration of enteric glial cell, that shows the ultrastructural morphology of the barrier system and can exclude Evan's blue dye, does not reasonably provide enablement for a method of treating any neurodegenerative disease (claim 15), such as multiple sclerosis by the induction of an appropriately functional blood brain barrier, mimicking the CNS blood brain barrier. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make and use the invention commensurate in scope with these claims.

21. The claims are drawn to a method of formation of a blood-brain barrier in the nervous system comprising the administration of Type II enteric glial cell, that are autologous in nature (claims 10-12), thereby treating any neurodegenerative disease, such as multiple sclerosis (claims 15-16).
22. The teachings of the specification and relevant literature are stated above. However, neither the post or prior art literature, nor the specification disclose any methods or working examples for inducing a blood brain barrier, thereby treating any neurodegenerative disease, for example multiple sclerosis (MS), by administering enteric glial cells. Undue experimentation would be required by one skilled in the art, to treat patients with all possible neurodegenerative disorders, by such method.
23. The art further teaches that the blood brain barrier (BBB) is a neurovascular unit, comprising cerebro-microvascular endothelial cells, astrocyte, supporting pericyte and neurons, that closely interact with one another to prevent the entry of more than 98% of the drugs into the brain parenchyma (Gumbleton et al. J Pharmac Soc 90: 1681-1698, 2001; page 1682, column 1, para 3; McCarty, Assay and Drug Dev Tech 3: 89-95, 2005; page 89, Introduction); by selection based on their lipid solubility and molecular size of 400-600 Da (Pardridge, J Neurochem 70: 1781-1792, 1998; page 1781, para 1). The art also teaches that various chemicals and peptides can induce changes in

permeability of the BBB (e.g. dexamethasone, cytokines etc.) (Grabb et al. J Neurosurgery, 82: 1053-1058, 1995; page 1057, column 1, para 2; Pardridge, J Neurovirol 5: 556-569, 1999; page 567, column 1, para 2). Finally, relevant art demonstrates that the BBB is disrupted due to common chronic ailments such as diabetes and various neurobiological diseases, like demyelinating diseases, that induce the "activation of inflammatory mechanisms, production of toxins and neurotrophins, and the breakdown of the BBB", further increasing the permeability into the CNS (Ballabh et al. Neurobiol of Dis 16: 1-13, 2004; page 9, column 2, para 4; Hawkins and Davis, Pharmacol Rev. 57: 173-185, 2005; page 182). The failure of clinical trials for treating complex immune-mediated chronic inflammatory demyelinating diseases, is due to axonal destruction, demyelination and the disruption of the blood brain barrier permeability, important factors that need experimentation for successful treatment of demyelinating diseases, such as MS (Comi et al., Clin Neurol and Neurosurg 108: 339-345, 2006; page 343, column 1, para 3; Said, Neuromus Disord 16: 293-303, 2006; Stangel, J Neurol Neurosurg Psychiat 72: 1-4, 2002; page 3, column 3, para 1). Based on the unpredictability of success, as seen from the post and prior art literature, undue experimentation would be required of the skilled artisan to indicate that the blood brain barrier induced by the administration of enteric glial cells will be functionally and physiologically comparable to the CNS barrier, and further provide a method for the treatment of any neurodegenerative disease or multiple sclerosis, with a reasonable expectation of success. In the absence of guidance regarding what

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other types of drugs, biological molecules, cells, etc. can be excluded or be transferred accross the brain parenchyma, the specification must provide such guidance commensurate in scope with the claims. The guidance has not been provided in the instant specification.

24. Due to the large quantity of experimentation necessary for inducing the formation of the blood brain barrier for the treatment of any neurodegenerative disease; the lack of direction/guidance presented in the specification regarding the same; the absence of working examples directed to same; the complex nature of the invention; the state of the prior and post art which has yet to determine treatment options for complex neurodegenerative disease, such as multiple sclerosis; and, unpredictability of the success of treatment of such diseases; undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

***Claim Rejections - 35 USC § 102***

25. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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26. Claims 1, 2, 10 and 11, are rejected under 35 U.S.C. 102(b) as clearly anticipated by Wang et al., (Soc Neurosc Abst Vol 27, pg 1562, published on August 2001).
27. The claims are drawn to a method of promoting functional regeneration of injured nerve fibres or the formation of a blood-brain barrier in the nervous system comprising the administration of Type II enteric glial cell (claims 10-11).
28. Wang et al. teach the injection of enteric glial cells (EG) in the dorsal root of the spinal cord after exposure of the lower thoracic spine and complete transection of the cord in rats. Wang et al. further teach that 3 weeks after transplantation, numerous regenerating dorsal root axons re-entered the spinal cord. Although the abstract does not specifically state that the EG cells were Type II subtype, this characteristic is an inherent property of the EG cells that are capable of promoting regeneration. Because the method steps disclosed by Wang et al. meet the method step limitations of claims 1, 2, 10 and 11, the method described in the reference anticipates the invention.
29. Claims 1, 2, 10 and 11, are rejected under 35 U.S.C. 102(b) as clearly anticipated by Khan et al., (Soc Neurosc Abst Vol 27, pg 2378, published on August 2001).

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30. The claims are drawn to a method of promoting functional regeneration of injured nerve fibres or the formation of a blood-brain barrier in the nervous system comprising the administration of Type II enteric glial cell (claims 10-11).

31. Khan et al. teach the transplantation EG cells subdurally into the spinal cords of adult rats, wherein the donor EG cells were identified by GFAP labeling. The reference further teach that the transplanted EG cells migrated from the graft into the spinal cord, and were ultrastructurally similar to astrocytes. Although the abstract does not specifically state that the EG cells were Type II subtype, this characteristic is an inherent property of the donor EG cells that were GFAP positive and similar to astrocytes . Because the method steps disclosed by Khan et al. meet the method step limitations of claims 1, 2, 10 and 11, the method described in the reference anticipates the invention.

32. Claims 1, 2, 10 and 11, are rejected under 35 U.S.C. 102(b) as clearly anticipated by Jiang et al., (Soc Neurosc Abst Vol 27, pg 1837, published on August 2001).

33. The claims are drawn to a method of promoting functional regeneration of injured nerve fibres or the formation of a blood-brain barrier in the nervous system comprising the administration of Type II enteric glial cell (claims 10-11).

34. Jiang et al. teach the injection of (Phaseolus vulgaris leucoagglutin) treated EG into the spinal cord of adult female rats, followed by intravenous



injection of Evan's Blue dye 1 week to 3 months post implantation. Using macroscopic examination and ultrastructure data, Jiang et al. demonstrated that tight junctions were fully formed by 2 months, that correlated with the observation that the capillaries vascularizing the graft were not permeable to the dye after 4 weeks of transplantation. Although the abstract does not specifically state that the EG cells were Type II subtype, this characteristic is an inherent property of the donor EG cells that had properties similar to astrocytes in inducing the formation of tight junctions. Because the method steps disclosed by Jiang et al. meet the method step limitations of claims 1, 2, 10 and 11, the method described in the reference anticipates the invention.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

35. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a

later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

36. Claims 3 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Khan et al., (Soc Neurosc Abst Vol 27, pg 2378, published on August 2001), or Jiang et al., (Soc Neurosc Abst Vol 27, pg 1837, published on August 2001), in view of Halfpenny et al. (Lancet Neurol 1: 31-40, May 2002).
37. Claims 3 and 12 recite that the enteric glial cells are autologous.
38. The teachings of Khan et al. and Jiang et al. are set forth above.
39. Khan et al. or Jiang et al. do not teach autologous enteric glia cells.
40. Halfpenny et al. state the use of autologous Schwann cells and oligodendrocyte progenitor cells for transplantation (page 33, column 2, para 1; page 34, column 1, para 1).
41. It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the method of administering donor enteric glia cells as taught by Khan et al. or Jiang et al., by using autologous cells as taught by Halfpenny et al. The person of ordinary skill in the art would have been motivated to use autologous cells because they provide ready availability and avoid the risk of graft rejection (Halfpenny et al., page 34, column 1, para 1). The person of ordinary skill in the art would have expected success because procedures for isolation of enteric glia and autologous cell transplantation were being performed at the time the invention was made.

42. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

### ***Conclusion***

43. No claims are allowed.
44. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aditi Dutt whose telephone number is (571) 272-9037. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:00 p.m.
45. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
46. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov/>. Should you have questions on access to the Private PAIR

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system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AD

10 April 2007

  
JANET L. ANDRES  
SUPERVISORY PATENT EXAMINER